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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,749	05/07/1999	THOMAS J. MEADE	A-58762-9/RF	3906

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EXAMINER

ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 04/29/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/306,749

Applicant(s)

MEADE ET AL.

Examiner

Stephanie Zitomer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Application status

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission and Reply to Office Action filed on March 14, 2002 have been entered..

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejection under 35 U.S.C. 101: Lack of specific asserted utility

2. Claims 12-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility. The specification fails to teach the claimed "phosphoramidite nucleoside comprising a covalently attached electron transfer moiety" and thus fails to disclose an asserted specific and substantial utility for the nucleoside. One of skill in the art would not have expected that a nucleoside with attached electron transfer moiety which comprises a transition metal as known in the art and taught in the specification would be readily incorporated during either an enzymatic synthesis or a chemical synthesis due to the bulky structure of such electron transfer groups which would interfere with the necessary contact between the reactants. For example, Bannwarth et al. (5,278,043) discloses nucleic acids in which electron transfer compounds are attached to the terminal nucleotides or are substituted for some of the internal nucleotides. Notably, the reference does not teach the incorporation of nucleosides with bulky electron transfer moieties attached thereto during nucleic acid synthesis. Therefore, the claimed nucleosides do not have an established utility. Furthermore, the specification teaches attachment of the electron transfer moiety to an amino-modified nucleotide after the modified nucleotide has been incorporated into the nucleic acid which teaches away from the claimed "nucleoside comprising a covalently attached electron transfer moiety". Note that because the claimed invention is not supported by a specific asserted utility for the reasons set forth above credibility cannot be assessed.

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Rejection under 35 U.S.C. 112, first paragraph: Lack of enablement

3. Claims 12-25 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Rejection under 35 U.S.C. 112, first paragraph: Lack of written description

4. Claims 12-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Although Figures 4A and 4B describe a nucleoside comprising a covalently attached electron transfer group, the specification fails to describe the claimed "nucleoside [or nucleotide] comprising a covalently attached electron transfer moiety". In the method of making nucleic acids comprising electron transfer moieties described in the specification at page 20 and in Example 1 at pages 37-40, the nucleosides are modified by addition of an amino group at the 2' or 3' position and the electron transfer moiety is attached via the amino group after synthesis of the nucleic acid in which the amino-modified nucleosides are incorporated (page 20, lines 10-18).

Furthermore, one of skill in the art would not have expected that a nucleotide with attached electron transfer moiety which comprises a transition metal as known in the art and taught in the specification would be readily incorporated during either an enzymatic synthesis or a chemical synthesis due to the bulky structure of such electron transfer groups which would interfere with the necessary contact between nucleotides. For example, Bannwarth et al. (5,278,043) discloses nucleic acids in which electron transfer compounds are attached to the terminal nucleotides or are substituted for some of the internal nucleotides. Nucleosides with bulky electron transfer moieties attached are not incorporated during nucleic acid synthesis. The present specification simply does not describe a phosphoramidite nucleoside with an electron transfer group attached thereto or a method of incorporating such nucleoside in a nucleic acid during synthesis. In addition to enablement the first paragraph of 112 requires a "written description". As set forth by the Court in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art

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"with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. It is clear from the lack of description in the specification that applicant did not contemplate the claimed nucleoside comprising a covalently attached electron transfer moiety at the time the claimed invention application was filed.

Response to applicant's traversal

5. Applicant's arguments filed March 14, 2002 have been fully considered but they are not persuasive. Initially, the arguments essentially repeat the arguments in the previous response, the Reply filed May 14, 2001 to the Office action of December 8, 2000. Again, passages in the specification are cited which teach modification of nucleotides and nucleosides with an amine group to which an ETM is attached after synthesis of the oligonucleotide. Regarding the description in the specification of "utilities of nucleic acids with ETMs", this is not an issue. As set forth above in paragraph 4, the lack of utility rejection applies to the claimed "nucleosides comprising a covalently attached electron transfer moiety at the 2' position" for which there is no asserted utility in the specification nor known utility in the prior art. Applicant has attached two articles as Exhibits A and B. The Handbook chapter of Exhibit A is not dated. Nevertheless, it may be noted that the ChromaTide nucleotides described therein are not relevant to the claimed nucleosides because in the nucleotides a fluorophore is attached to the **nucleotide base** via a 4-carbon linker and may additionally contain a 7-to-10 atom spacer whereas in the claimed nucleosides the ETM is attached directly to the **ribose** via an amine modifying group. The Exhibit B paper by Hurley et al., published in 1998, well after the 1993 effective filing date of the application, describes the incorporation during automated DNA synthesis of a nucleotide comprising a polypyridine-metal complex. In this paper too, the metal complex is attached to a base and Scheme 1 suggests that attachment is through a linker. However, as the Supporting Information containing experimental details was not provided, this cannot be ascertained with certainty. Most notably, Hurley et al. state that "[a] direct method for the site-specific incorporation of metal complexes during solid-phase oligonucleotide synthesis **has never been reported**" (emphasis added) which negates the argument that Exhibits A and B constitute prior art. Thus, the Hurley et al. paper in particular supports the examiner's position that neither the specification nor the prior art provides enablement or

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written description as to how to make the claimed nucleosides comprising a ribose comprising a covalently attached ETM at the 2' position and its utility for incorporation during oligonucleotide synthesis.

Provisional double patenting obviousness-type rejection

6. The Provisional double patenting obviousness-type rejection of claims 12-25 over claims 21-28 of co-pending Application No. 09/602,618 set forth at paragraph 5 of the final Office action mailed August 13, 2001 has been withdrawn in view of applicant's Terminal Disclaimer filed March 14, 2002.

Conclusion

7. **No claim is allowed.**

8. This is an RCE of applicant's earlier Application No. 09/306,749. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone

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number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact Patent Analyst Tiffany Tabb at 703-605-1238.



Stephanie Zitomer, Ph.D.

April 17, 2002

STEPHANIE ZITOMER
PRIMARY EXAMINER